

**REMARKS**

By this amendment, claims 1, 6, 7, and 11-13 are amended. These amendments are made to even more clearly recite the claimed invention, do not add prohibited new matter and are fully supported by the specification. Support for these amendments may be found, for example, on page 11, lines 17 through 19, of the specification. Reconsideration and withdrawal of the rejections in the outstanding Office Action are respectfully requested in view of the foregoing amendments and the following remarks.

**Information Disclosure Statements**

Applicants note that the Examiner lined through item 6 on the Form PTO-1449 for the Information Disclosure Statement dated June 8, 2006. The Examiner asserts that it is not clear which of the documents in item 6 should be considered. In response, Applicants hereby submit a new PTO Form 1449, listing U.S. Patent Application No. 09/985,652. Applicants submit that no additional fee is required, as this PTO Form 1449 merely clarifies the description of an item previously brought to the attention of the Office. Applicants respectfully request the Examiner to acknowledge consideration of these documents by initialing the attached PTO Form 1449.

**Claim Rejections – 35 U.S.C. § 101**

The Office Action asserts that claims 1, 6, 7, and 11-13 are directed to non-statutory subject matter, alleging that the claims do not recite a physical transformation of matter. Without agreeing with or acquiescing to the rejection, Applicants note that the claims have been amended, and that the

amendments address any alleged § 101 deficiencies. Applicants respectfully request withdrawal of the rejection.

Claim Rejections – 35 U.S.C. § 112, First Paragraph

The Office Action rejects claims 1, 6, 7, and 11-13 under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the enablement requirements. The Examiner asserts that the “specification does not teach particular conditions which must be met to select a compound as a lead-candidate (i.e. to single out any particular compound as being a ‘better’ ligand than the others, or which binds more tightly than another, etc).”

Without agreeing with or acquiescing to the rejection, Applicants note that the claims have been amended to recite “judging similarity of partial structures of the query molecule and the trial compound based on two-dimensional graphs of the query molecule and the trial compound where each atom is represented as a node and each covalent bond is represented as an arc.” Applicants also submit that the specification clearly defines the conditions for selecting lead candidate compounds; the specification lists the specific steps and parameters used in selecting lead candidate compounds on pages 10 through 13. Accordingly, Applicants submit that both the claims and the specification enable one skilled in the art to make and use the claimed invention.

Claim Rejections – 35 U.S.C. § 112, Second Paragraph

The Office Action rejects claims 1, 6, 7, and 11-13 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite.

The Examiner asserts that claim 1 is indefinite because it is allegedly unclear whether the “trial compound” or the “query molecule” is intended to be the lead candidate compound. Without agreeing with or acquiescing to the rejection, Applicants note that the claims have been amended to recite “selecting at least one lead-candidate compound capable of binding as a ligand to a protein from a database *of trial compounds*.” Applicants submit that the claims clearly indicate that the lead candidate compounds are selected from among a database of trial compounds (rather than query molecules). Accordingly, Applicants respectfully request withdrawal of the rejection.

The Examiner rejects claims 6 and 7 because there is allegedly no antecedent basis for “the compounds” (recited in lines 2-3 of claims 6 and 7). Without agreeing with or acquiescing to the rejection, Applicants note that the claims 6 and 7 have been amended to recite “wherein the compound database comprises information on three-dimensional structures of the trial compounds.” The Examiner also alleges that the term “the lead candidate compound” in claim 6 has no antecedent basis. Without agreeing with or acquiescing to the rejection, Applicants note that claim 6 has been amended. Line 3 of claims 6 and 7 has also been amended to recite, “wherein step (b) further comprises” to further clarify the claims.

The Office Action also rejects claims 6 and 7 because step (e) allegedly does not indicate what is being screened for or against. Without agreeing with or acquiescing to the rejection,

Applicants note that claims 6 and 7 have been amended to recite “screening the lead-candidate compounds capable of binding as a ligand to the protein.”

The Examiner also asserts that the recitation “binding scheme to the protein of the query molecule” in claim 6 is unclear. Without agreeing with or acquiescing to the rejection, Applicants note that claim 6 has been amended to recite the “binding scheme of the query molecule to the protein.”

The Examiner also asserts that the phrase “based on correspondence of the partial structures of the query molecular and the [trial] compound” in claim 6 is unclear. Specifically, the Examiner alleges that it is not clear what is based on correspondence of the query molecule and trial compound. The Examiner also alleges that the required degree of similarity is not clear from the claims.

In response, Applicants submit that it is clear from the claims that the “binding scheme of the lead-candidate compound” may be estimated “based on the correspondence of the partial structures of the query molecule and the trial compound.” Furthermore, the term “degree of similarity” is clearly defined throughout the specification. For example, the specification (*e.g.*, page 10, fourth paragraph, through page 11, first paragraph, of the specification) indicates that

Selection of the trial compound is performed by comparing each parameter between each of the query molecules and the trial compound. A trial molecule for which any one of the parameters is too much different from that of the query molecule beyond acceptable criteria is rejected as a candidate for the second screening. For this purpose, it is generally necessary to specify an upper limit and/or a lower limit for each parameter. For example, if the difference of the parameter of total number of atoms is represented as [number of atoms in query molecule]-[number of atoms in trial molecule], and the lower limit of the difference of the parameter is defined as -3 and the upper limit as +2, molecules having number of atoms lower by 3 to higher by 2 compared with the query molecules will be selected. However, there may be

parameters which do not require such limits, and such parameters are optionally excluded from selection criteria. As for certain parameters such as number of atoms for each chemical element, selection can be performed by using a secondary parameter such as that derived by adding the number of nitrogen atoms and the number of oxygen atoms.

This screening process is further explained on page 11, paragraphs 2-3, of the specification, which discusses a “second screening by matching of the trial compounds selected in the first screening with the query molecules for the mode of covalent bond can be performed” and correspondence of query and trial compounds depicted in two-dimensional graphs where each atom is represented as a node and each covalent bond is represented as an arc (*see, e.g.*, page 11 of the specification). Accordingly, Applicants submit that the specification clearly defines the scope of the claims, and respectfully request withdrawal of the rejection.

The Examiner further alleges that it is unclear what is “based on information of three-dimensional structures” in step (c) in claim 7. Applicants submit that it is clear from the step (c) that the *ligand binding site* is “based on information of three-dimensional structures” of the ligands. Furthermore, the specification (*e.g.*, page 14, lines 5-11, of the specification) clearly indicates that

In order to estimate a virtual receptor model..., for example, shape and properties of a ligand binding site of the biopolymer may be estimated based on the information of a specific known ligand known to be capable of binding to the biopolymer...such as shape, hydrogen bonding, electrostatic potential and the like correspond well in the three-dimensional space.

Accordingly, Applicants submit that the scope of this claim element is clear, both from the claim language and the specification, and respectfully request withdrawal of the rejection.

The Office Action also rejects claim 7, alleging that it is “unclear what parameters must be included or what relationship is intended between elements in order for (something) to be ‘based on’

3D information.” Applicants submit that the specification clearly explains the relationship between estimating the ligand binding site, estimating the virtual receptor model, and the three-dimensional structures of the ligands. For example, the excerpt of the specification cited above clearly explains the interrelationship between these claim elements (*see, e.g.*, page 14, lines 5-11, of the specification). Accordingly, Applicants submit that the scope of this claim element is clear, from both the claim language and the specification, and respectfully request withdrawal of the rejection.

Lastly, the Examiner alleges that claims 11-13 are unclear because the claims do not indicate where or when in claim 1 the constructing step is intended to occur. Without agreeing with or acquiescing to the rejection, Applicants note that the claims has been amended to recite “wherein step (a) further comprises...” Applicants respectfully request withdrawal of the rejection.

#### Claim Rejections – 35 U.S.C. § 102

The Office Action rejects claims 1, 6, 7, and 11-13 under 35 U.S.C. 102(b) as being anticipated by Wang et al. (J. Med. Chem., Vol. 37, pp. 4479-4489 (1994), hereinafter “WANG”). In response, Applicants respectfully submit that WANG does not anticipate the claimed invention.

The claims require “judging similarity of partial structures of the query molecule and the trial compound based on two-dimensional graphs of the query molecule and the trial compound where each atom is represented as a node and each covalent bond is represented as an arc.” Although the Examiner asserts that “WANG inherently includes ‘matching modes of covalent bonds’ because the method disclosed in WANG considers certain covalent bond lengths in the pharmacophore of the query compound and trial compounds in the database,” WANG does not judge the similarity of query

molecules “based on two-dimensional graphs of the query molecule and the trial compound where each atom is represented as a node and each covalent bond is represented as an arc,” as required by the claims. For at least this reason, WANG does not disclose all of the elements of the claimed invention.

Applicants respectfully submit that WANG does not anticipate the claimed invention, and request withdrawal of the rejection.

### **CONCLUSION**

In view of the foregoing, it is submitted that the Examiner’s rejections should be withdrawn. Entry and consideration of the present amendment, reconsideration of the outstanding Office Action, and allowance of the present application and all of the claims therein are respectfully requested and now believed to be appropriate.

Although it is within the discretion of the Examiner to enter amendments made after a Final Office Action, Applicants submit that the amendments clarify previously recited claim elements, do not raise new issues, and should not necessitate a new search. Accordingly, Applicants respectfully request that the Examiner enter the amendments. Applicants have made a sincere effort to place the present application in condition for allowance and believe that she has done so.

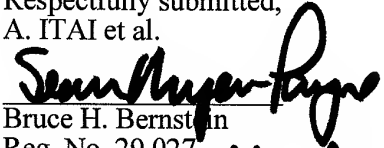
Any amendments to the claims which have been made in this amendment, and which have not been specifically noted to overcome a rejection based upon the prior art, should be considered to have been made for a purpose unrelated to patentability, and no estoppel should be deemed to attach thereto.

Should the Commissioner determine that any additional extension of time is required in order to render this response timely and/or complete, a formal request for an extension of time, under 37 C.F.R. §1.136(a), is herewith made in an amount equal to the time period required to render this response timely and/or complete. The Commissioner is authorized to charge any required extension of time fee under 37 C.F.R. §1.17 to Deposit Account No. 19-0089.

If the Examiner has any questions, or wishes to discuss this matter, the Examiner is respectfully requested to contact the undersigned at the below-listed telephone number.

June 14, 2007  
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Respectfully submitted,  
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